AMENDMENT

Please amend the application without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

In the Specification

Please delete page i.

Please amend page 1, line 1, of the application as follows:

-- ~~ADHESION MOLECULES~~

TITLE OF THE INVENTION

ADHESION MOLECULES

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of International Application PCT/GB02/00107 filed on January 11, 2002 and published as WO 02/062845 on August 15, 2002, which application claims priority from Great Britain Application 0100750.9 filed January 11, 2001.

Each of the foregoing applications, and each document cited or referenced in each of the foregoing applications, including during the prosecution of each of the foregoing applications and ("application cited documents"), and any manufacturer's instructions or catalogues for any products cited or mentioned in each of the foregoing applications and articles and in any of the application cited documents, are hereby incorporated herein by reference. Furthermore, all documents cited in this text, and all documents cited or referenced in documents cited in this text, and any manufacturer's instructions or catalogues for any products cited or mentioned in this text or in any document hereby incorporated into this text, are hereby incorporated herein by reference. Documents incorporated by reference into this text or any teachings therein may be used in the practice of this invention. Documents incorporated by reference into this text are not admitted to be prior art.

It is noted that in this disclosure and particularly in the claims, terms such as "comprises", "comprised", "comprising" and the like can have the meaning attributed to it in U.S. Patent law; e.g., they can mean "includes", "included", "including", and the like; and that terms such as

"consisting essentially of" and "consists essentially of" have the meaning ascribed to them in U.S. Patent law, e.g., they allow for elements not explicitly recited, but exclude elements that are found in the prior art or that affect a basic or novel characteristic of the invention.

FIELD OF THE INVENTION

This invention relates to novel proteins, termed AAC74854.1, AAC76768.1 and P10155 herein identified as adhesion molecules and to the use of these proteins and nucleic acid sequences from the encoding genes in the diagnosis, prevention and treatment of disease.

~~All publications, patents and patent applications cited herein are incorporated in full by reference.~~ --

Please amend the paragraph beginning on page 18, line 24, as follows:

-- The functionally-equivalent polypeptides of the first aspect of the invention may be polypeptides that are homologous to the ADS1, ADS2, or ADS5 polypeptides or to[[the]] the adhesion molecule regions of the ADS1, ADS2, or ADS5 polypeptides. Two polypeptides are said to be "homologous", as the term is used herein, if the sequence of one of the polypeptides has a high enough degree of identity or similarity to the sequence of the other polypeptide. "Identity" indicates that at any particular position in the aligned sequences, the amino acid residue is identical between the sequences. "Similarity" indicates that, at any particular position in the aligned sequences, the amino acid residue is of a similar type between the sequences. Degrees of identity and similarity can be readily calculated (Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing. Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). --

Please amend the paragraph beginning at page 20, line 5, as follows:

-- Percentage identity, as referred to herein, is as determined using BLAST version 2.1.3 using the default parameters specified by the NCBI (the National Center for Biotechnology

Information; see NCBI website ~~http://www.ncbi.nlm.nih;gov/~~) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1]. --

Please amend the paragraph beginning at page 21, line 27, as follows:

-- By "significant structural homology" is meant that the Inpharmatica Genome Threader™ predicts two proteins, or protein regions, to share structural homology with a certainty of at least 10% more preferably, at least 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% and above. The certainty value of the Inpharmatica Genome Threader™ is calculated as follows. A set of comparisons was initially performed using the Inpharmatica Genome Threader™ exclusively using sequences of known structure. Some of the comparisons were between proteins that were known to be related (on the basis of structure). A neural network was then trained on the basis that it needed to best distinguish between the known relationships and known not-relationships taken from the CATH structure classification ~~(www.biochem.ucl.ac.uk/bsm/cath)~~(see the CATH Protein Structure Classification website). This resulted in a neural network score between 0 and 1. However, again as the number of proteins that are related and the number that are unrelated were known, it was possible to partition the neural network results into packets and calculate empirically the percentage of the results that were correct. In this manner, any genuine prediction in the Biopendium search database has an attached neural network score and the percentage confidence is a reflection of how successful the Inpharmatica Genome Threader™ was in the training/testing set. --

Please amend the paragraph beginning at page 25, line 8, as follows:

-- Homologues include those polypeptide molecules that possess greater than 30% identity with the ADS1, ADS2 or ADS5 regions of the ADS1, ADS2 and ADS5 polypeptides, respectively. Percentage identity is as determined using BLAST version 2.1.3 using the default parameters specified by the NCBI (the National Center for Biotechnology Information; see NCBI website ~~http://www.ncbi.nlm.nih;gov/~~) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1]. Preferably, variant homologues of polypeptide fragments of this aspect of the invention have a degree of sequence identity with the ADS1, ADS2, and ADS5 adhesion molecule regions of the ADS1, ADS2, and ADS5 polypeptides, respectively, of greater than 40%. More preferred variant polypeptides have degrees of identity of greater than 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99%, respectively with the ADS1, ADS2, and ADS5 and

adhesion molecule regions of the ADS1, ADS2, or ADS5 polypeptides, provided that said variants retain activity as an adhesion molecule. Variant polypeptides also include homologues of the truncated forms of the polypeptide fragments discussed above, provided that said variants retain activity as an adhesion molecule. --

Please amend the paragraph beginning at page 34, line 11, as follows:

-- Percentage identity, as referred to herein, is as determined using BLAST version 2.1.3 using the default parameters specified by the NCBI (the National Center for Biotechnology Information; see NCBI website ~~http://www.ncbi.nlm.nih;gov/~~). --

Please amend the paragraph beginning at page 57, line 3, as follows:

-- Protocols such as ELISA, RIA, and FACS for measuring polypeptide levels may additionally provide a basis for diagnosing altered or abnormal levels of polypeptide expression. Normal or standard values for polypeptide expression are established by combining body fluids or cell extracts taken from normal mammalian subjects, preferably humans, with antibody to the polypeptide under conditions suitable for complex formation. The amount of standard complex formation may be quantified by various methods, such as by photometric means. --

Please amend the paragraph beginning at page 66, line 15, as follows:

-- The National Center for Biotechnology Information (NCBI) Genbank protein database is then viewed to examine if there is any further information that is known in the public domain relating to AAC76768.1 (ADS2). This is the U.S. public domain database for protein and gene sequence deposition (FIG. 13). AAC76768.1 (ADS2) is an Escherichia Coli sequence, its Genbank protein ID is AAC76768.1 and it is 427 amino acids in length. AAC76768.1 (ADS2) was cloned by a group of scientists at the University of ~~Wisconssin~~ Wisconsin, USA. The entry identifies AAC76768.1 (ADS2) as a hypothetical protein. The public domain information for this gene does not annotate it as an adhesion molecule. --

Please amend paragraph 11 on page 72 as follows:

-- A fragment or functional equivalent according to any one of paragraphs 1-10, which has greater than 30% sequence identity with an amino acid sequence as recited in any one of SEQ ID NO:2, SEQ ID NO:4 and SEQ ID NO:6, or with a fragment thereof that possesses adhesion molecule activity, preferably greater than 40%, 50%, 60%, 70%, 86%5 90%7 95%, 98% or 99%

sequence identity, as determined using BLAST version 2 3 using the default parameters specified by the NCBI (the National Center for Biotechnology Information; see NCBI website ~~http://www.ncbi.nlm.nih;gov/~~) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1]. --